

REMARKS

The Official Action of May 29, 2003, and the prior art cited and relied upon therein have been carefully reviewed. The claims in the application remain as claims 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90 and 92, and of these claims 54, 56, 58, 60, 62, 64, 66, 68 and 70 have not been rejected (this is so in spite of the Office Action summary, the allowability of these claims having been confirmed in a telephone conference with Examiner Weber on July 1, 2003). As regards the remaining claims commencing with claim 72, the applicants respectfully submit that these claims are also directed to patentable subject matter and should be allowed. Accordingly, applicants respectfully request favorable reconsideration regarding the rejected claims, and allowance thereof.

The attorney docket for the present application for the present attorneys of record is "GABIZON=1". The attorney docket number appearing on PTO papers is the attorney docket number for previous attorneys of record, and applicants respectfully request the PTO to correct the PTO records and henceforth use "GABIZON=1" as the attorney docket number for this application.

The examiner continues to hold that claims 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92 (for the purpose of clarity hereinafter designated as "rejected claims") are rejected under §103 as obvious from Ostro et al EP 546,951 (Ostro) in view of Kedar's publication (*Journal of Immunotherapy*, 1994, vol 16, pp. 47-59). This rejection is respectfully traversed.

The rejection states that Kedar et al "... found meager improvement in pharmacokinetics (MLV-IL2 was only slightly better than free soluble IL2 in a T-cell

proliferation assay), but were somewhat displeased that the non-SSLs were rapidly removed by the RES. The rapid removal by RES is exactly what it is argued as desired by the instantly claimed method."

While the rejection correctly notes parts of the results presented by Kedar et al, it is not clear to applicants (who include two of the authors of the Kedar citation) how the PTO arrives at the conclusion that "rapid removal by RES is exactly what it is argued as desired by the instantly claimed method." Thus, applicants respectfully disagree with the allegation that these results in combination with the disclosed Ostro citation can form the basis for the instant invention. The results presented in Kedar could not suggest to a person skilled in the art that such a liposomal preparation would be effective in a combination therapy when administered according to the method of claim 72.

In other words, even if the combination of Ostro and Kedar were obvious, this combination would not have reached the claimed method of claim 72, i.e. there is no *prima facie* obviousness. There is also, of course, no indication, suggestion or teaching in either of the cited documents that the claimed combination therapy would work, i.e. there is no reasonable expectation of success, let alone any improvement.

Furthermore, the rejection states that the specification provides no evidence to support the synergistic effects alleged, which are present in the instant invention. Applicants respectfully invite the examiner's attention to pages 7-11 of the specification and specifically to Tables I-IV where the effectiveness of the combination treatment is shown to be substantially greater than a combination of the effects of the individual treatments. For example, Group 5 in Table I resulted in eight survivals out of eight total mice, a

greater survival rate than what could have been predicted and more than the additive of Groups 4 and 6. Similarly, improved results are shown comparing Group 3 with the additive effects of Groups 2 and 6.

Table II shows the Group 5 survival rate of seven out of nine mice, far more than the additive effects from Groups 3 and 4. Applicants believe that it is clear from these data, and from the data of the following Tables III and IV as well, that a synergistic effect is indeed produced according to the present invention, and this is a result which certainly would not have been obvious to the person of ordinary skill in the art at the time the present invention was made. Stated another way, the prior art provides no reasonable expectation of obtaining results even approaching those achieved according to the present invention.

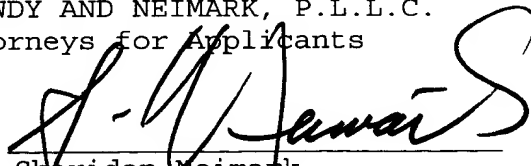
Applicants respectfully request a withdrawal of the rejection based on section 103.

A review of claim 72 has revealed a redundancy near the end of the claim. The amendment presented above eliminates this redundancy. Such amendment is clearly "cosmetic" and non-narrowing.

Applicants respectfully request favorable reconsideration as regards the rejection based on Section 103, entry of the amendment presented above, and early formal allowance.

Respectfully submitted,
BROWDY AND NEIMARK, P.L.L.C.
Attorneys for Applicants

By


Sheridan Weimark
Registration No. 20,520